

Continuation of U.S.S.N. 09/298,084

Filed: May 3, 2001

PRELIMINARY AMENDMENT

ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5. Many other peptides may be used apart from the specifically enumerated sequences here.

In the Claims

1. (Amended) A [matrix] <u>drug delivery composition</u> comprising:
a substrate [capable of providing attachment of a heparin-binding peptide];
a peptide comprising a [binding] domain that binds heparin <u>or heparin-like compounds</u>
with high affinity,

wherein the peptide is covalently bound to the substrate so that the heparin binding domain is able to bind to heparin or heparin-like compounds;

heparin or a heparin-like polymer; and

a protein growth factor or a peptide fragment thereof having a domain that binds heparin with low affinity, wherein low affinity is defined as not binding with heparin at a NaCl concentration of between about 25 mM and 140 mM.

Please cancel claim 2.

- 3. (Three times Amended) The [matrix] composition of claim 1 wherein the domain of the growth factor or peptide fragment thereof is further defined as comprising a length of about 8 to 30 amino acid residues comprising at least 2 basic amino acid residues, a ratio of basic to acidic amino acid residues of at least 2, and a ratio of hydrophobic amino acid residues to basic amino acid residues of at least 0.67.
- 4. (Amended) The [matrix] <u>composition</u> of claim 3 wherein the basic amino acid residues are K or R.

ATL1383635v1

Filed: May 3, 2001

PRELIMINARY AMENDMENT

5. (Amended) The [matrix] <u>composition</u> of claim 3 wherein the acidic amino acid residues are further defined as D or E.

6. (Amended) The [matrix] composition of claim 3 wherein the hydrophobic amino acid residues are further defined as A, V, F, P, M, I, or L or C when C is involved in a disulfide bond.

7. (Three times Amended) The [matrix] <u>composition</u> of claim 1 wherein the growth factor or peptide fragment thereof is selected from the group consisting of neurturin, persephin, IGF-1A, IGF-1β, EGF, NGFβ, NT-3, BDNF, NT-4, [TGF-β2,] TGF-β3, [or] <u>and</u> TGF-β4.

Please cancel claims 8-19.

20. (Amended) The [matrix] <u>composition</u> of claim 66 wherein the substrate comprises fibrin.

21. (Amended) The [matrix] <u>composition</u> of claim 66 wherein the substrate comprises a synthetic polymer hydrogel.

24. (Amended) The [matrix] <u>composition</u> of claim 64 wherein the heparin or heparinlike polymer has a molecular weight between about 3,000 and 10,000,000 Daltons.

25. (Amended) The [matrix] <u>composition</u> of claim 64 wherein the heparin-like polymer is a polysaccharide having a molecular weight between about 3,000 and 10,000,000 Daltons, and having at least one negative charge per two saccharide rings and no more than one positive charge per ten saccharide rings.

ATL1383635v1

ETH 108 13248/13



Continuation of U.S.S.N. 09/298,084

Filed: May 3, 2001

PRELIMINARY AMENDMENT

- 26. (Amended) The [matrix] <u>composition</u> of claim 64 wherein the heparin-like polymer is <u>selected from the group consisting of</u> dextran sulfate, chondroitin sulfate, heparin sulfate, fucan, alginate, [or] <u>and</u> a derivative thereof.
- 27. (Three times Amended) The [matrix] <u>composition</u> of claim 1 wherein the molar ratio of heparin or heparin-like polymer to growth factor <u>or peptide fragment thereof</u> is at least one.

Please cancel claims 29-56.

57. (Amended) [A] The composition of claim 1 in a vascular graft [comprising a matrix capable of supporting cell adhesion, said matrix comprising

bound heparin or heparin-like polymer and a growth factor having a low binding affinity for heparin].

- 58. (Amended) [An] <u>The composition of claim 1 in an</u> article for treatment of dermal wounds [comprising a matrix capable of supporting cell adhesion, said matrix comprising bound heparin or heparin-like polymer and a growth factor having low binding affinity for heparin].
- 59. (amended) The [article] <u>composition</u> of claim 58, wherein the growth factor is TGF-β.

Please cancel claim 60.

61. (Amended) [An] The composition of claim 1 in an implantable sterilized composition [comprising

Continuation of U.S.S.N. 09/298,084

Filed: May 3, 2001

PRELIMINARY AMENDMENT

a matrix capable of supporting cell adhesion, said matrix comprising bound heparin or a heparin-lie polymer and a growth factor or peptide fragment thereof having low binding affinity for heparin].

62. (Amended) A method for providing controlled release of <u>a</u> growth factor comprising:

preparing a [matrix comprising a growth factor having a domain with a low affinity for binding heparin and bound heparin or heparin-like polymer] composition comprising

a substrate,

a peptide comprising a domain that binds heparin or heparin-like compounds, wherein the peptide is covalently bound to the substrate so that the heparin binding domain is able to bind to heparin or heparin-like compounds,

heparin or a heparin-like polymer, and

a growth factor or a peptide fragment thereof having a domain with low affinity for binding heparin and bound heparin or heparin-like polymer, wherein low affinity is defined as not binding with heparin at a NaCl concentration of between about 25 mM and 140 mM; and

placing the composition on a wound in need thereof.

63. (Amended) The method of claim 62, wherein the growth <u>factor or a peptide</u> <u>fragment thereof</u> is released by dissociation of [a component of the matrix] the growth factor from the heparin or heparin-like <u>polymer</u>.

5

Please add new claims 64 and 65.

ETH 108 13248/13